mark with methanol. Place a 2-milliliter aliquot into a 15-milliliter centrifuge tube and evaporate to dryness on a steam bath with a stream of dry air. Dissolve the residue in 1 milliliter of dry pyridine. Calculate the lincomycin content as follows:

$$\text{Lincomycin content in milligrams per milliliter} = \frac{R_u \times W_s \times d \times f}{R_s \times \text{number of milliliters of sample}}$$

where:

$$R_u = \frac{\text{Area of lincomycin sample peak}}{\text{Area of internal standard}}$$

$$R_s = \frac{\text{Area of lincomycin standard peak}}{\text{Area of internal standard}}$$

W_s=Weight of lincomycin working standard in milligrams;
d=Dilution factor;
f=Potency of lincomycin working standard in milligrams of lincomycin per milligram

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) [Reserved]

(4) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter, using a solution containing 0.5 milligram of lincomycin per milliliter.

(5) *Depressor substances.* Proceed as directed in § 436.35 of this chapter.

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

[39 FR 19161, May 30, 1974, as amended at 46 FR 3841, Jan. 16, 1981; 46 FR 60568, Dec. 11, 1981; 50 FR 19921, May 13, 1985]

Subparts D–E [Reserved]

Subpart F—Dermatologic Dosage Forms

§ 453.522 Clindamycin phosphate dermatologic dosage forms.

§ 453.522a Clindamycin phosphate topical solution.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Clindamycin phosphate is a solution of clindamycin phosphate in a suitable and harmless vehicle. Each milliliter contains 10 milligrams of clindamycin activity. Its clindamycin content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of clindamycin that it is represented to contain. Its pH is not less than 4.0 and not more than 7.0. The clindamycin phosphate used conforms to the standards prescribed by § 453.22(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The clindamycin phosphate used in making the batch for clindamycin content, microbiological activity, moisture, pH, crystallinity, and identity.

(*b*) The batch for clindamycin content and pH.

(ii) Samples required:

(*a*) The clindamycin phosphate used in making the batch: 6 packages, each containing approximately 300 milligrams.

(*b*) The batch: A minimum of six immediate containers.

(b) *Tests and methods of assay*—(1) *Clindamycin content* (*vapor phase chromatography*). Proceed as directed in § 436.304 of this chapter, except prepare the sample for assay and calculate the clindamycin content as follows:

(i) *Preparation of the sample.* Accurately transfer a volume of sample equivalent to approximately 20 milligrams of clindamycin activity to a 50-milliliter volumetric flask. Evaporate the sample to near dryness under a stream of nitrogen. Dilute to 50 milliliters with pH 9.0 borate buffer and mix well. Place 25.0 milliliters of this solution into a 50-milliliter stoppered centrifuge tube. Add 10 milliliters of chloroform. Shake vigorously for 15 minutes and centrifuge to obtain adequate phase separation of the chloroform and aqueous phase. Transfer 20 milliliters of the aqueous phase from the tube into a 35-milliliter stoppered centrifuge tube. Add to the tube a weighed

amount of intestinal alkaline phosphatase equivalent to 50 units of activity[1] and allow to stand until the phosphatase has dissolved completely. Place the centrifuge tube into a water bath at 37° C ± 2° C for 2.5 hours. After the 2.5-hours hydrolysis, allow the solution to cool.

(ii) *Calculations.* Calculate the clindamycin content as follows:

$$\text{Clindamycin content per milliliter} = (R_u \times W \times_s \times d \times f)/(R_s \times V)$$

where:

R_u=Area of clindamycin sample peak/Area of internal standard;
R_s=Area of clindamycin standard peak/Area of internal standard;
W_s=Weight of clindamycin working standard in milligrams;
d=Dilution factor;
f=Potency of clindamycin working standard in milligrams of clindamycin per milligram;
V=Volume of sample in milliliters.

(2) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted drug.

[46 FR 2997, Jan. 13, 1981. Redesignated at 54 FR 38224, Sept. 15, 1989]

§ 453.522b Clindamycin phosphate gel.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Clindamycin phosphate gel contains clindamycin phosphate in a suitable and harmless vehicle. Each gram contains clindamycin phosphate equivalent to 10 milligrams of clindamycin activity. Its clindamycin content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of clindamycin that it is represented to contain. Its pH is not less than 4.5 and not more than 6.5. It passes the identity test. The clindamycin phosphate used conforms to the standards prescribed by § 453.22(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification: samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The clindamycin phosphate used in making the batch for clindamycin content, microbiological activity, moisture, pH, crystallinity, and identity.

(B) The batch for clindamycin content, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The clindamycin phosphate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(B) The batch: A minimum of six immediate containers.

(b) *Tests and methods of assay*—(1) *Clindamycin content (High performance liquid chromatographic assay).* Proceed as directed in § 436.216 of this chapter, using ambient temperature, an ultraviolet detection system operating at a wavelength of 210 nanometers, a 25-centimeter long x 4.6-millimeter ID column packed with microparticulate (5 to 10 micrometers in diameter) reversed phase octysilane hydrocarbon bonded silica packing material, a flow rate of about 1.0 milliliter per miunute, and a known injection volume of between 10 and 20 microliters. The retention time of clindamycin phosphate, and clindamycin are approximately 6 and 9 minutes, respectively. Reagents, working standards and sample solutions, resolution test solution, system suitability requirements, and calculations are as follows:

(i) *Reagents*—(A) *0.1M Potasium phosphate monobasic buffer.* Dissolve 13.61 grams of potassium phosphate monobasic in 775 milliliters of water. Adjust the pH to 2.5 with phosphoric acid. Further dilute with water to a volume of 1,000 milliliters.

(B) *Mobile phase.* Mix 225 milliliters of acetonitrile and 775 milliliters of 0.1*M* potassium phosphate, pH 2.5 buffer (225:775). Filter through a suitable filter capable of removing particulate matter greater than 0.5 micron in diameter. Degas the mobile phase just prior to its introduction into the chromatograph.

(ii) *Preparation of working standard, sample, and resolution test solutions*—(A)

[1] Defined such that 50 units hydrolyzes at least 20 micromoles of a clindamycin phosphate authentic sample under the assay conditions described in § 436.304 of this chapter.